

### IN THE CLAIMS

Please amend the claims as follows:

1. (Original) A system, comprising:
  - a transdermal drug delivery device;
  - an implantable cardiac rhythm management (CRM) device communicatively coupled to the transdermal drug delivery device, the implantable CRM device including:
    - an ischemia detector producing an ischemia indicating signal;
    - a drug level detector producing an indication of a blood drug concentration; and
    - a drug delivery controller coupled to the ischemia detector and the drug level indicator; and
    - an external device communicatively coupled to the implantable CRM device, the external device including an external user input receiving an external user command,
  - wherein the drug delivery controller controls the transdermal drug delivery device based on at least one of the ischemia indicating signal, the indication of the blood drug concentration, and the external user command.
2. (Original) The system of claim 1, wherein the implantable CRM device comprises a sensing circuit to sense at least one electrogram.
3. (Original) The system of claim 2, wherein the ischemia detector comprises an input coupled to the sensing circuit and an ischemia analyzer to produce the ischemia indicating signal based on an analysis of the at least one electrogram.
4. (Original) The system of claim 1, wherein the ischemia detector comprises:
  - an impedance sensor to sense an electrical impedance signal; and
  - an ischemia analyzer to produce the ischemia indicating signal based on an analysis of the electrical impedance signal.

5. (Original) The system of claim 1, wherein the ischemia detector comprises:
- an accelerometer to sense an acceleration signal; and
  - an ischemia analyzer to produce the ischemia indicating signal based on an analysis of the acceleration signal.
6. (Original) The system of claim 1, further comprising:
- a remote device receiving signals including at least one of the external user command and the at least one electrogram; and
  - a network coupled between the external device and the remote device to provide for bidirectional communication between the external device and the remote device.
7. (Original) The system of claim 6, wherein the remote device comprises an emergency response module adapted to contact an emergency response unit in response to the external user command.
8. (Original) The system of claim 6, wherein the remote device comprises a remote signal processor to process the received signals using at least one predetermined algorithm.
9. (Original) The system of claim 8, wherein the remote device further comprises a remote user interface providing for monitoring of the processed received signals and entry of remote user commands.
10. (Original) The system of claim 9, wherein the remote device further comprises a remote device controller generating commands controlling one or more of the transdermal drug delivery device, the implantable CRM device, and the external device based on the received signals and the remote user commands.
11. (Original) The system of claim 1, wherein the drug level indicator comprises a blood drug level detector to measure the blood drug concentration.

12. (Original) The system of claim 1, wherein the drug level indicator comprises a respiratory sensor to sense a respiratory signal as the indication of the blood drug concentration.

13. (Original) The system of claim 1, wherein the drug level indicator comprises a heart rate detector to determine a heart rate as the indication of the blood drug concentration.

14. (Original) The system of claim 1, wherein the transdermal drug delivery device comprises a drug reservoir containing one or more pharmaceutical agents shifting a source of metabolically synthesized energy for cardiac contractions from fatty acid to glucose.

15. (Original) The system of claim 14, wherein transdermal drug delivery device further comprises at least one skin contact electrode for transdermal drug delivery.

16. (Original) The system of claim 14, wherein the one or more pharmaceutical agents comprise one or more of agents decreasing, inhibiting, and/or reducing fatty acid oxidation and agents increasing, enhancing, and/or stimulating pyruvate, glucose, and/or lactate oxidation.

17. (Original) The system of claim 16, wherein the one or more pharmaceutical agents further comprise one or more of anti-hypertensive agents, anti-arrhythmic agents, pressors, vasopressors, vasodilators, anti-hyperlipidemic agents, anti-anginal agents, inotropic agents, diuretics, volume expanders, thrombolytics, anti-platelet agents, beta-blockers, angiotensin converting enzyme (ACE) inhibitors, and angiotensin receptor blockers.

18. (Currently Amended) A system, comprising:

an implantable metabolic sensor to sense a metabolic signal indicative of a cardiac metabolic level;

an implantable processor coupled to the implantable metabolic sensor, the implantable processor including:

a metabolic sensor processing circuit to determine the cardiac metabolic level

from the metabolic signal; and

a drug delivery controller producing a drug delivery signal based on the cardiac metabolic level; and

an implantable drug delivery device, communicatively[[,]] coupled to the implantable processor, to deliver a drug based on the drug delivery signal, the implantable drug delivery device including a drug reservoir storing a drug shifting a source of metabolically synthesized energy for cardiac contractions from fatty acid to glucose.

19. (Original) The system of claim 18, further comprising:

a remote device receiving signals including at least one of the metabolic signal and the cardiac metabolic level; and

a network coupled between the external device and the remote device to provide for bidirectional communication between the external device and the remote device.

20. (Original) The system of claim 19, wherein the remote device comprises a remote signal processor to process the received signals using at least one predetermined algorithm.

21. (Original) The system of claim 20, wherein the remote device further comprises a remote user interface providing for monitoring of the processed received signals and entry of remote user commands.

22. (Original) The system of claim 21, wherein the remote device further comprises a remote device controller generating commands controlling one or more of the implantable metabolic sensor, the implantable processor, the implantable drug delivery device based on the received signals and the remote user commands.

23. (Original) The system of claim 18, wherein the implantable metabolic sensor comprises a pH sensor.

24. (Original) The system of claim 18, wherein the implantable metabolic sensor comprises an oxygen pressure ( $\text{PO}_2$ ) sensor.

25. (Original) The system of claim 18, wherein the implantable metabolic sensor comprises a carbon dioxide pressure ( $\text{PCO}_2$ ) sensor.

26. (Original) The system of claim 18, wherein the implantable metabolic sensor comprises a glucose sensor.

27. (Original) The system of claim 18, wherein the implantable metabolic sensor comprises a creatine sensor.

28. (Original) The system of claim 18, wherein the implantable metabolic sensor comprises a C-creative protein sensor.

29. (Original) The system of claim 18, wherein the implantable metabolic sensor comprises a creatine kinase sensor.

30. (Original) The system of claim 18, wherein the implantable metabolic sensor comprises a creatine kinase-MB sensor.

31. (Original) The system of claim 18, wherein the implantable drug delivery device comprises a reservoir drug level detector, coupled to the drug reservoir, to produce a drug-level-low alert signal indicative of a low reservoir drug level.

32. (Currently Amended) The system of claim 18, further comprises a drug-eluting stent coupled to the implantable drug delivery device, ~~wherein the implantable drug delivery device is communicatively coupled to the implantable processor.~~

33. (Original) The system of claim 18, wherein the implantable processor and the implantable drug delivery device are housed within a single implantable housing.

34. (Original) The system of claim 33, further comprises a drug eluting endocardial lead coupled to the implantable drug delivery device, the drug eluting endocardial lead including at least one drug eluting electrode configured to be disposed within one of a coronary sinus and a portion of a great cardiac vein adjacent to a left ventricle.

35. (Original) The system of claim 33, further comprises a drug eluting epicardial lead coupled to the implantable drug delivery device, the drug eluting epicardial lead including at least one drug eluting electrode configured to be attached to a portion of an epicardial wall.

36. (Original) The system of claim 18, wherein the drug comprises one or more of agents decreasing, inhibiting, and/or reducing fatty acid oxidation and agents increasing, enhancing, and/or stimulating pyruvate, glucose, and/or lactate oxidation.

37. (Original) The system of claim 36, wherein the one or more pharmaceutical agents further comprises one or more of anti-hypertensive agents, anti-arrhythmic agents, pressors, vasopressors, vasodilators, anti-hyperlipidemic agents, anti-anginal agents, inotropic agents, diuretics, volume expanders, thrombolytics, anti-platelet agents, beta-blockers, angiotensin converting enzyme (ACE) inhibitors, and angiotensin receptor blockers.

38. (Original) A method, comprising:

- detecting an ischemia using an implantable cardiac rhythm management (CRM) device
- executing an automated ischemia detection algorithm;

- detecting an external user command directing a drug delivery, the external user command transmitted to the implantable CRM device from an external device;

- producing a drug delivery signal upon the detection of at least one of the ischemia and the external user command;

- transmitting the drug delivery signal to an transdermal drug delivery device; and
- delivering a drug from the transdermal drug delivery device.

39. (Original) The method of claim 38, wherein detecting the ischemia comprises:

- sensing at least one electrogram; and

- detecting the ischemia by using an automated algorithm analyzing the electrogram.

40. (Original) The method of claim 38, wherein detecting the ischemia comprises:

- sensing an electrical impedance signal; and

- detecting the ischemia by using an automated algorithm analyzing the electrical impedance signal for abrupt changes in electrical impedance.

41. (Original) The method of claim 38, wherein detecting the ischemia comprises:

- sensing an acceleration signal indicative of a heart motion; and

- detecting the ischemia by using an automated algorithm analyzing the acceleration signal for abrupt decreases in amplitude.

42. (Original) The method of claim 38, further comprising:

- receiving the external user command by the external device; and

- transmitting the external user command from the external device to a remote device though a network connecting the external device and the remote device.

43. (Original) The method of claim 42, further comprising notifying an emergency response unit upon reception of the external user command by the remote device.

44. (Original) The method of claim 42, further comprising transmitting at least a portion of the at least one electrogram from the external device to a remote device through a network connecting the external device and the remote device.

45. (Original) The method of claim 44, further comprising:

notifying a remote user;

receiving a remote user command directing the drug delivery at the remote device;

transmitting the remote user command from the remote device to the external device through the network;

transmitting the remote user command from the external device to the implantable CRM device; and

detecting the remote user command transmitted from the external device to the implantable CRM device.

46. (Original) The method of claim 45, wherein producing the drug delivery signal comprises producing a drug delivery signal upon the detection of at least one of the ischemia, the external user command, and the remote user command.

47. (Original) The method of claim 38, wherein transmitting the drug delivery signal to the transdermal drug delivery device comprises transmitting through a telemetry link between the implantable CRM device and the transdermal drug delivery device.

48. (Original) The method of claim 38, wherein transmitting the drug delivery signal to the transdermal drug delivery device comprises transmitting a voltage signal representing the drug delivery signal via tissue conduction.

49. (Original) The method of claim 38, wherein delivering the drug comprises delivering one or more pharmaceutical agents shifting a source of metabolically synthesized energy for cardiac contractions from fatty acid to glucose.

50. (Original) The method of claim 49, wherein delivering the drug comprises releasing one or more of agents decreasing, inhibiting, and/or reducing fatty acid oxidation and agents increasing, enhancing, and/or stimulating pyruvate, glucose, and/or lactate oxidation.

51. (Original) The method of claim 50, wherein delivering the drug further comprises releasing one or more of anti-hypertensive agents, anti-dysrhythmic agents, pressors, vasopressors, vasodilators, anti-hyperlipidemic agents, anti-anginal agents, ionotropic agents, diuretics, volume expanders, thrombolytics, anti-platelet agents, beta-blockers, angiotensin converting enzyme (ACE) inhibitors, and angiotensin receptor blockers.

52. (Original) The method of claim 38, further comprising verifying whether a sufficient amount of the drug has been delivered.

53. (Original) The method of claim 52, wherein verifying whether the sufficient amount of the drug has been delivered comprises detecting a signal indicative of a concentration of the drug in blood.

54. (Original) The method of claim 53, wherein detecting the signal indicative of a concentration of the drug in blood comprises at least one of:

- measuring a blood drug concentration;
- sensing a respiratory signal; and
- measuring a heart rate.

55. (Original) The method of claim 54, further comprises;

producing an insufficiency alert signal if the concentration of the of the drug in blood is below a predetermined level;

transmitting the insufficiency alert signal from the transdermal drug delivery device to the implantable CRM device;

detecting the insufficiency alert signal transmitted from the transdermal drug delivery device to the implantable CRM device; and

wherein producing the drug delivery signal comprises producing a drug delivery signal upon the detection at least one of the ischemia, the external user command, and the insufficiency alert signal.

56. (Original) A method, comprising:

sensing a metabolic signal using an implantable sensor;

determining a cardiac metabolic level based on the metabolic signal using an implantable processor connected to the implantable sensor;

producing a drug delivery signal based on the cardiac metabolic level; and

delivering a drug from an implantable drug delivery device, upon receipt of the drug delivery signal, to shift a source of metabolically synthesized energy for cardiac contractions from fatty acid to glucose.

57. (Original) The method of claim 56, further comprising:

determining whether the cardiac metabolic level exceeds a predetermined threshold level;

and

producing a drug delivery signal when the cardiac metabolic level exceeds a predetermined threshold level.

58. (Original) The method of claim 56, wherein sensing the metabolic signal comprises sensing a blood pH level.

59. (Original) The method of claim 56, wherein sensing the metabolic signal comprises sensing a blood oxygen pressure ( $PO_2$ ).

60. (Original) The method of claim 56, wherein sensing the metabolic signal comprises sensing a blood carbon dioxide pressure ( $PCO_2$ ).

61. (Original) The method of claim 56, wherein sensing the metabolic signal comprises sensing a blood glucose level.

62. (Original) The method of claim 56, wherein sensing the metabolic signal comprises sensing a blood creatine level.

63. (Original) The method of claim 56, wherein sensing the metabolic signal comprises sensing a blood C-creative protein level.

64. (Original) The method of claim 56, wherein sensing the metabolic signal comprises sensing a blood creatine kinase level.

65. (Original) The method of claim 56, wherein sensing the metabolic signal comprises sensing a blood creatine kinase-MB level.

66. (Original) The method of claim 56, further comprising transmitting at least one of the metabolic signal and the cardiac metabolic level to a remote device though a network.

67. (Original) The method of claim 66, further comprising:  
sensing at least one electrogram from the heart; and  
transmitting at least a portion of the at least one electrogram to the remote device through the network.

68. (Original) The method of claim 67, further comprising:

- notifying a user by using the remote device;
- receiving a remote user command directing the drug delivery at the remote device;
- transmitting the remote user command from the remote device to the implantable processor through the network; and
- detecting the remote user command transmitted from the external device to the implantable processor,
- wherein producing the drug delivery signal comprises producing the drug delivery signal based on at least one of the cardiac metabolic level and the remote user command.

69. (Original) The method of claim 68, further comprising:

- monitoring a level of the drug stored in the drug delivery device; and
- transmitting an drug-level-low alert signal to the remote device when the level of the drug stored in the drug delivery device is below a predetermined minimum level.

70. (Original) The method of claim 56, wherein transmitting the drug delivery signal comprises transmitting the drug delivery signal through a telemetry link between the implantable processor and the drug delivery device.

71. (Original) The method of claim 56, wherein transmitting the drug delivery signal comprises transmitting the drug delivery signal via electrical conduction through tissue intervening the implantable processor and the drug delivery device.

72. (Original) The method of claim 56, wherein delivering the drug from the implantable drug delivery device comprises delivering the drug through a drug eluting stent.

73. (Original) The method of claim 56, wherein delivering the drug from the implantable drug delivery device comprises delivering the drug through a lead having an endocardial drug eluting electrode.

74. (Currently Amended) The method of claim 56, wherein delivering the drug from the implantable drug delivery device comprises delivering the drug through a lead having an epicardial drug eluting lead electrode.

75. (Original) The method of claim 56, wherein delivering the drug comprises releasing one or more of agents decreasing, inhibiting, and/or reducing fatty acid oxidation and agents increasing, enhancing, and/or stimulating pyruvate, glucose, and/or lactate oxidation.

76. (Original) The method of claim 75, wherein delivering the drug further comprises releasing one or more of anti-hypertensive agents, anti-dysrhythmic agents, pressors, vasopressors, vasodilators, anti-hyperlipidemic agents, anti-anginal agents, ionotropic agents, diuretics, volume expanders, thrombolytics, anti-platelet agents, beta-blockers, angiotensin converting enzyme (ACE) inhibitors, and angiotensin receptor blockers.

77. (Original) The method of claim 56, further comprising verifying whether a sufficient amount of the drug has been delivered.

78. (Original) The method of claim 77, wherein verifying whether a sufficient amount of the drug has been delivered comprises:

sensing a response metabolic signal using the implantable sensor;

determining a response cardiac metabolic level based on the response metabolic signal using the implantable processor connected to the implantable sensor; and

determining whether the sufficient amount of the drug has been delivered by determining whether the response cardiac metabolic level is below a predetermined threshold.